\* ~ 1/4/04/04/001440

### 1 of 55

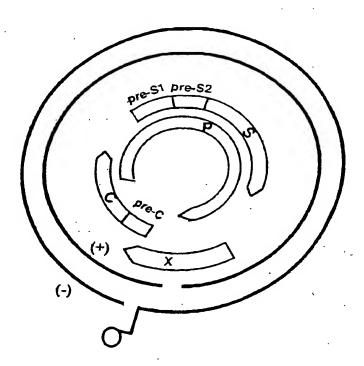


Figure 1

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Figure 2

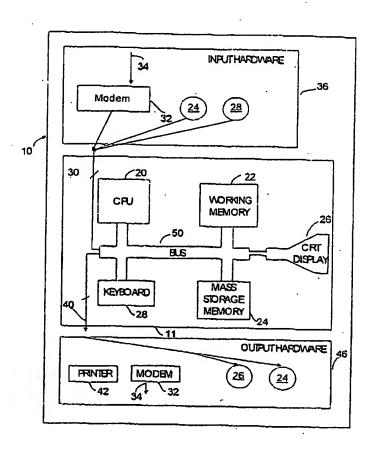


Figure 3A

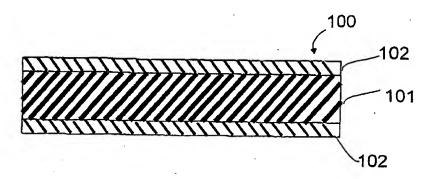


Figure 3B

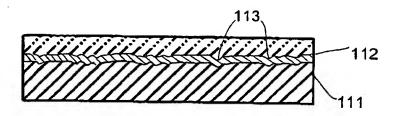


Figure 3C

# Angeline Ingrid Bartholomeusz et al. HBV VARIANTS DETECTION AND APPLICATION Docket: 19781 Sheet 5 of 55

Figure	4:	Patient	A nt	sequence			
			10	20	1 30	40	5.0
		GCTTC	CACCA	ATCGGCAGGCA	AGGAAGACAGC	4 U የጥልርጥርርር አጥ	50
					-00,210110A0C	CIACICCCAI	CTCTCCACC
			.60	70	80	90	100
		TCTAAC	AGACA	GTCATCCTCA	GGCCATGCAG	ひと でころなってでころ	100
						TOURNETCER	GCACATTCC
			110	120	130	140	150
		ACCATO	CTCTC	CTAGATCCCA	GACCTGCTGG	₽ĠĠĊŦĊĊŶĠŦ	TOUT TOUTONAUN
						TOGGICCAGI	CCGGAACA
,			160	170	180	190	200
		GTAAAC	CCTGT	TCCGACTACT	GCCTCTCCCA:	PATCGTCAAn	200 ***********************************
					5,0 2 0 0 1.	00101111	CITCICGAG
			210		230	240	250
		GACTGG	GGACC	CTGCGCCGAA	TATGGAGAGC	ACCACATCAC	ጋር ያ ርዕጥጥሮር የአር
							DATICCIAG
			260	270	280	290	300
		GACCCC	TGCTC	GTGTTACAGG	CGGGGTTTTTC	TTGTTGACAZ	OUC OTOOTE AGA
							CANTOCIC
,			310	320	330	. 340	350
		ACAATA	CCAAA	Gagtctagac <sup>*</sup>	rcgrggtggac	TTCTCTCAAT	סטנ בסמדימיתיתי
			360	370	380	390	400
		GGGAGC	ACCCA	CGTGTCCTGG	CAAAATTTGC	AGTCCCCAAC	CTCCAATC
			410	420	430	440	450
		ACTCAC	CAACC	rcttgtcctc	CAATTTGTCCT	GGTTATCGCT	GGATGTGT
					• •		
			460	470		490	500
		CTGCGG	GTTTI	PATCATCTTCC	TCTTCATCCT	GCTGCTATGC	CTCATCTT
			510	520	530	540	550
		CTTGTTG	GTTCT	TTCTGGACTAC	CAAGGTATGT	TGCCCGTTTG	TCCTCTAC
			560	570	580	590	600
		TTCCAGG	AACAI	CAACTACCAG	CACGGGACCA	TGCAAGACCT	GCACGACT
			610	620	630	640	650
		CCTGCTC	AAGGA	ACCICTAIGT	TTCCCTCTTG	TTGCTGTACA	AAACCTTC
			660	670	680	690	700
		GGACGGA	Aattg	CACTTGTATT	CCCATCCCAT	CATCTTGGGC	TTCGTAA
			710	720	730	740	750
		GATTCCT	ATGGG	AGTGGGCCTC	AGTCCGTTTCT	CCTGGTTCAC	. στη Απτή
			760	770	780	790	800
		GTGCCAT	TTGTT	CAGTGGTTCG <sup>1</sup>	TAGGGCTTTCC	CCCACTGTTT	ያርር ተጥጥር
				•			
		i	810	820	830	840	850
							, <del>-</del> -

## Angeline Ingrid Bartholomeusz et al. HBV VARIANTS DETECTION AND APPLICATION Docket: 19781 Sheet 6 of 55

AGTTATATG	GATGATGTGGTA1	TTGGGGGCCAAG	rctgtacaac:	ATCTTGA
860	0 870	880	890	. 900
ATCCCTTTA	PACCGCTATTACC	CAATTTTTTTTAA	GTCTTTGGGT1	ATACATT
910	) 920	930	940	950
TAAACCCTAA	ATAAAACCAAGCG	TTGGGGCTACTC	CCTTAACTTO	CATGGGA
960	) 970 <sup>.</sup>	980	990	1000
TATGTAATTO	GGAAGTTGGGGTA	CCTTGCCACAGG	AACATATTGT	'ACAAAA
AATCAAA				• •

Figure 4

## Angeline Ingrid Bartholomeusz et al. HBV VARIANTS DETECTION AND APPLICATION Docket: 19781 Sheet 7 of 55

Figure	5:	Patient	A.	HBV	Polymerase	sequence
--------	----	---------	----	-----	------------	----------

10	. 20	30	40	50
EDWGPCAEYGEHHI	RIPRTPARVI	rggvflydknp	HNTKESRLV	DFSQFS
60	70	80	90	100
RGSTHVSWPKFAVP	NLQSLTNLLS	SSNLSWLSLDV	Saafyhlpli	HPAAMPH
110	120	130	140	150
LLVGSSGLPRYVAR	LSSTSRNINY	QHGTMQDLHD	SCSRNLYVSI	LLLLYKT
160	170	· 180	190	200
FGRKLHLYSHPIIL	GFRKIPMGVG	LSPFLLVQFT:	SAICSVVRRA	FPHCLA
210	220	230	240	250
FSYMDDVVLGAKSVÇ	OHLESLYTAI	TNFLLSLGIHI	LNPNKTKRWG	YSLNFM
260 GYVIGSWGTLPQEHI	270 VQKIK			

Figure 5

# Angeline Ingrid Bartholomeusz et al. HBV VARIANTS DETECTION AND APPLICATION Docket: 19781 Sheet 8 of 55

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Figure	6:	Patient	A	HBV	HbsAg	sequence
--------	----	---------	---	-----	-------	----------

10	20	30 -	40	50
MESTTSGFLGPLLV	/LQAGFFLLTI	RILTIPKSLDS	SWWTSLNFLGG	APTCPG
60	70	80	90	100
QNLQSPTSNHSPTS	SCPPICPGYR	MCLRRFIIFI	LFILLLCLIFL	LVLLDY
110	120	130	140	150
QGMLPVCPLLPGTS	STTSTGPCKTO	CTTPAQGTSME	FPSCCCTKPSD	GNCTCI
160	170	180	190	200
PIPSSWAFVRFLWE	Wasvrfswfs	SLLVPFVQWFV	GLSPTVWLSV	IWMMWY
210 WGPSLYNILNPFIP	220 LLPIFFCLWV	YYI		

## Angeline Ingrid Bartholomeusz et al. HBV VARIANTS DETECTION AND APPLICATION Docket: 19781 Sheet 9 of 55

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#### Figure 7: Patient B HBV NT sequence

	4	•		
10	20	30	40	50
TCTGTCTCCACCTT	TGAGAGACA	CTCATCCTCAC	GCCATGCAG	TOGAACT
60 .	70	80	90	100
CCACAACCTTCCAC	CAAACTCTG	CAAGATCCCAC	AGTGAGAGG	CCTGTAT
110	120	130	140	150
TTCCCTGCTGGTGG	CTCCAGTTC.	aggaacagta <i>i</i>	<i>ACCCTGTTC</i>	CGACTTC
160	170	180	100	0.00
TGTCTCTCACACAT	TIU マンカルマンサンツ・	┲ĊͲĊĊŊĊĊŊͲſſ IJŨ	790	200
10101010110110110	corchater	ICICGAGGAII	.GGGGTCCCT(	CGCTGA
210	220	230	240	250
ACATGGAGAACATC	ACATCAGGA'	TTCCTAGGACC	₽₽₽ ₽₽₽₽₽₽₽₽₽	מסט מידים המכי
				i inong
260	270	280	290	300
GCGGGGTTTTTCTT	ettgacaag:	AATCCTCACAA	TACCGCAGAG	TCTAGA
310	320	330	340	350
CTCGTGGTGGACTT	TCTCAATT	ITCTAGGGGGA	ACTACCGTG1	GTCTTG
3.50				
360	370	380	390	400
GCCAAAATTCGCAGT	CCCCAACC	ICCAATCACTC	ACCAACCTCC	TGTCCT
410	430	420	440	
CCAACTTGTCCTGGT	42U TTADOCCTC	430	440	450
004101101001001	TATOGCIGO	MIGIAICIGC	GGCGTTTTAT	CATCTT
460	470	480	490	E 0.0
CCTCTTCATCCTGCT	GCTATGCCT	プログラング プログラング・ファック	でからでもなった。 なないないない。 なない。	でになって中
			-100110110	IGGACI
510	520	530	540	550
ATCAAGGTATGTTGC	CCGTTTGT	CTCTAATTCC	AGGATCTTCA	ACCACC
560	570	580	590	600
AGCACGGGACCATGC	AGAACCTGC	CACGACTCCTG	CTCAAGGAAA	CTCTAT
•	•			
610	620	630	640	650
GTATCCCTCCTGTTG	CTGTACCA	ACCTTCGGAC	ggaaattgca	CCTGTA
4.40				
660	670	680	690	700
TTCCCATCCCATCAT	CTGGGCTI	TCGGAAAATT	CCTATGGGAG	TGGGCC
710	720	722		
	/ 4 U 'かこここのころ こっ	730	/40	750
TCAGCCCGTTTCTCC	A GGCTCAGI	TIACTAGTGC	CATTTGTTCA	GTGGTT

# Angeline Ingrid Bartholomeusz et al. HBV VARIANTS DETECTION AND APPLICATION Docket: 19781 Sheet 10 of 55

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76		770	780	790	800
CGTAGGGCT		ACTGTTTGGC	FTTCAGTTAT	ATGGATGATGI	GGT
81		820	830	840	850
ATTGGGGGG		STATCGCATC	PTGAGTCCCT	PTTTACCGCTG	STTA
8 6	. •	870	880	890	900
CCAATTTTC		TTTGGGTATAC	CATTTAAACCO	CTCACAAAACA	AAA
91		920	930	940	950
AGATGGGGI		CACATTTCATO	GGCTATGTC	ATTGGATGTTA	TGG
96 GTCATTGCC		970 CACATCAGACA	980 AGAAAA		

### Figure 7 continued

# Angeline Ingrid Bartholomeusz et al. HBV VARIANTS DETECTION AND APPLICATION Docket: 19781 Sheet 11 of 55

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### Figure 8: Patient B POLYMERASE sequence

10	20	. 30	40	50
EDWGPCAEHGEHHI	RIPRTPARV	IGGVFLVDKNE	PHNTAESRLVV	DFSQFS
60	70	80	90	100
RGNYRVSWPKFAVP	NLQSLTNLL:	SSNLSWLSLDV	Saafyhlplh	PAAMPH
110	120	130	140	150
LLVGSSGLSRYVAR	Lssnsrifni	HQHGTMQNLHD	SCSRKLYVSL	LLLYQT
160	170	180	190	200
FGRKLHLYSHPIIL	Gerkipmgvo	GLSPFLLAQFT	SAICSVVRRA	FPHCLA
210	220	230	240	250
FSYMDDVVLGAKSV	SHLESLFTAV	TNFLLSLGIH	LNPHKTKRWG	HSLHFM
260 GYVIGCYGSLPQDH	IRQK	. '		

## Angeline Ingrid Bartholomeusz et al. HBV VARIANTS DETECTION AND APPLICATION Docket: 19781 Sheet 12 of 55

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#### Figure 9: Patient B HBsAG sequence

10 .	20 .	30	40	· 50
MENITSGFLGPLLVL	QAGFFLLTR1	LTIPQSLD	SWWTSLNFLGG	TVCLG
60				
60	70	80	90	100
QNSQSPTSNHSPTSCI	PPTCPGYRWM	YLRRFIIF:	LFILLLCLIFLI	CALLDA
110	120	130	140	150
QGMLPVCPLIPGSSTT	STGPCRTCT	TPAQGNSM	YPSCCCTKPSDO	NCTCI
160	170	180	190	200
PIPSSWAFGKFLWEWA	SARFSWLSL	LVPFVQWF	/GLSPTVWLSVI	YWMWWY
210	220			
WGPSLYRILSPFLPLI	PIFFCLWVY	I		-

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Figure 10

# Angeline Ingrid Bartholomeusz et al. HBV VARIANTS DETECTION AND APPLICATION Docket: 19781 Sheet 14 of 55

•	•			
710	720		740	750
TTGTATTCCCATC	CCATCATCTT	GGGCTTTCGC	AAGATTCCTA	TGGG DCT
				LOGGAGI
760	770	780	790	800
GGGCCTCAGTCCG	TTTCTCCTGG	CTCAGTTTACT	PAGTGCC74000	000
		oronorranc,	INGIGCCATT!	LGTTCAG
810	222			
810	820	830	840	850
TGGTTCGTAGGGC	TTTCCCCCAC	TGTTTGGCTTT	TAGTTATAT	CATCAT
				JORIGAI
860	870	880	000	
-			890	900
GTGGTATTGGGGG	CCAAGTCTGT	ACAACAYCTTO	AATCCCTTTI	TACCGC
910	920	930	940	950
TGTTACCAATTTT			UPC	930
	0111101011	IGGGIAIACAI	TTAAACCCTA	CTAAAA
960	970	980	990	1000
CCAAACGTTGGGG	CTACTCCCTT	AACTTCATGGG	ייים או איים שיים ביים ביים	2000
			WILL GIVAL!	GGAAGT
1010	1000	2000		
	1020	1030	1040	
TGGGGTACCTTAC	Cacaagaaca:	<b>PATTGTACACA</b>	AAATCAGACA	А

Figure 10 continued

# Angeline Ingrid Bartholomeusz et al. HBV VARIANTS DETECTION AND APPLICATION Docket: 19781 Sheet 15 of 55

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Figure 11: Patient C Polymera	se sequence
-------------------------------	-------------

10 EDWGPCTEHGER	20 HIRIPRTPARVT	30 GGVFLVDKNI	40 PHNTTESRLVV	50 DESOFS
60	70	80	90	1.00
RGNTQVSWPKF	AVPNLQSLTNLLS	SNLSWLSLD	/SAAFYHLPLH	PAAMPH
110 LLVGSSGLPRYV	120 ARLSSTSRNINY	130 OHGTMODI.HI	140	150
160	170	180		
	ILGFRKIPMGVG		190 SAICSVVRRA	200 FPHCLA
210	220	230	240	250
FSYMDDVVLGAR	SVQHLESLFTAV	TNFLLSLGII	ILNPTKTKRWG	YSLNFM
260 GYVIGSWGTLPQ	270 EHIVHKIRQ	- '		•

## Angeline Ingrid Bartholomeusz et al. HBV VARIANTS DETECTION AND APPLICATION Docket: 19781 Sheet 16 of 55

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### Figure 12 Patient C HbsAg sequence

10	20	30	40	50
MESTTSGFLGPLLA	LQAGFFLLT	RILTIPQSLDS	WWTSLNFLGO	Stpkcpg
60	70	80	90	WGLLDY
QNLQSPTSNHSPTSO	CPPICPGYR	WMCLRRFIIFL	FILLLCLIFI	
· 110	120	130	140	150
QGMLPVCPLLPGTS1	TSTGPCKT	CTTPAQGTSMF	PSCCCTKPSE	GNCTCI
160	170	180	190	200
PIPSSWAFARFLWEW	Masvrfswl	SLLVPFVQWFVO	GLSPTVWLLV	IWMMWY
210 WGPSLYNXLNPFLPL	220 LPIFFCLW	VYI		

Figure 12

## Angeline Ingrid Bartholomeusz et al. HBV VARIANTS DETECTION AND APPLICATION Docket: 19781 Sheet 17 of 55

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### Figure 13; Patient D NT sequence

racient D MI	sequence			
10	20	20		
	ACCAATCGGCAG	30 TCACCARGA	40	50
		1 CAGGAAGAC	AGCCTACTCC	CATCTCT
60	70	80	90	
CCACCTCTAAGA	AGACAGTCATCC	TCAGGCCATG	JU Cactedace	100
				CCACAAC
110	120	130	140	150
TTTCCACCAAGO	TCTGCTAGATC	CCCGAGTGAG	GGGCCTCTAT	TTTCCTG
CTGGTGGCTCC2	170	180	190	200
CTGGTGGCTCCA	IGT T C C G G G A C A C	TAAACCCTG	TTCCGACTAC	rgcctct.
210	220	230	0.40	
CCCATATCGTCA	ATCTTCTCGAGG	Z 30 FACTGGGGAC	240	250
			CIGCACTGA	ACATGGA
260	270	280	290	300
GAGCACAACATC	AGGATTCCTAGG	ACCCCTGCT	CGTGTTACAGO	೦೦೮ ಇಂಗಾವನಿ
				2000101
310	320	330	340	350
TTTTCTTGTTGA	CAAGAATCCTCA	CAATACCAC	AGAGTCTAGAC	CTCGTGG
	370			
TGGACTTCTCTC	טיט AATTTTTACCC	38U CDDCCDCCC	390	400
	11101AGGG	GAAGCACCCG	CGTGTCCTGG	CCAAAA
410	420	430	440	450
TTCGCAGTCCCC	AACCTCCAATCA	CTCACCAACC	TCTTGTCCTC	450
460	470	480 -	490	500
GTCCTGGCTATCC	CTGGATGTGTC:	IGCGGCGTTT	TATCATCTTC	CTCTTC
ATCCTGCTGCTAT	520	530	540	550
ATCCTGCTGCTAT	.occicateTic	TTGTTGGTTC	TTCTGGATTA	CCAAGG
560	570	580	500	
TATGTTGCCCGTT	TGTCCTCTACT	CCAGGAACG	ングリ アピカカビザカごごカ	600
			CAACIACCA	GCACGG
610	620	630	640	650
GACCATGCAAGAC	CTGCACGATTCC	TGCTCAAGG	AACCTCTATG	0.00 רחיירירים
• 🔨				iliçee
660	670	680	690	700
TCATGTTGCTGTA	CAAAACCTTCGG	ACGGAAACT	SCACTTGTAT1	CCCAT
710				-
	720 6Cでででとこへ れこれ	730	740	750
CCCATCATCCTGG	CCITICGCAAGA	ATTUUTATGG	SAGTGGGCCTC	AGTCC

## Angeline Ingrid Bartholomeusz et al. HBV VARIANTS DETECTION AND APPLICATION Docket: 19781 Sheet 18 of 55

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760	770	780	790	800
GTTTCTCTTGACT	CCAGTTTACTAG	TGCCATTTG	TCAGTGGTT	CGTAGGG
810	820	830	840	850
CTTTCCCCCACTO	STTTGGCTTTCA	GTTATATGG	NTGATGTGGT	ATTGGGG
860	870	088	890	900
GCCAAGTCTGTAC	CAACATCTTGAG	TCCTTTATA	CCGCTATTA	CAATTT
· 910	920	930	940	950
TCTTTTGTCTTTG	GGTATACATTT	AAACCCTAAT	'Aaaccaago	GATGGG
960	970	980	990	1000
GTTACTCCCTTAA	CTTCATGGGAT	ATGTCATTGG	AAGTTGGGG	SACTTTA
1010 CCACAGGAACATA	1020 TTGTGCTC			

Figure 13 continued

## Angeline Ingrid Bartholomeusz et al. HBV VARIANTS DETECTION AND APPLICATION Docket: 19781 Sheet 19 of 55

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### Figure 14: patient D HBV POL sequence

10	20	30	40	50
EDWGPCTEHGE	HNIRIPRTPARVI	GGVFLVDKN	PHNTTESRLVV	DFSQFS
60	70	80	90	100
RGSTRVSWPKF	AVPNLQSLTNLLS	SNLSWLSI:D	VSAAFYHLPLH	PAAMPH
110	120	130	140	150
LLVGSSGLPRYY	Varlsstsrnvny	Qhgimodlh	DSCSRNLYVSLI	MLLYKT
160	170	180	190	200
FGRKLHLYSHP	Ilgfrkipmgvg	LSPFLLTQF	TSAICSVVRRAJ	PHCLA
210	220	230	240	250
FSYMDDVVLGAR	SVQHLESLYTAI	Infllslgie	RLNPNKTKRWG)	SLNFM
260 GYVIGSWGTLPQ	EHIVL			

Figure 14

## Angeline Ingrid Bartholomeusz et al. HBV VARIANTS DETECTION AND APPLICATION Docket: 19781 Sheet 20 of 55

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### Figure 15 Patient D HBsAg sequence

10	20	30	40	50
MESTTSGFLGPLLVI	LQAVFFLLT	RILTIPQSLDS	SWWTSLNFLGE	SAPACPG
60	70	80	90	TATTDA
QNSQSPTSNHSPTSC	PPICPGYR	WMCLRRFIIFI	FILLLCLIFL	100
110	120	130	140	150
QGMLPVCPLLPGTST	TSTGPCKT	CTIPAQGTSMF	PSCCCTKPSD	GNCTCI
160 PIPSSWAFARFLWEW	170 ASVRFS*L	180 SLLVPFVQWFV	190 GLSPTVWLSV	200 Ywmwyi
210 WGPSLYNILSPFIPL	220 LPIFFCLW	/YI		

Figure	16:	Patient	E RB	V nt	seq	uence			
	10	2 AGGCCATGC	:0		30		40		So
AGTCATC	CTC	GGCCATGC	AGTG	SAAC'	CCA	GCACAT	TCCA	.CCLAGO	OTCT
	60								
GCTAGAT	CCCA	.gagtgagg	י הפרריו	מתמס	ያህ ግጥጥ	Concor	90		100
							GGTG	GCTCCA	GTT
	110	12	0	1	.30		140		150
CAGGAAC	AGTA	AACCCTGT	TCCGA	CTAC	TGC	CTCTCC	CATA	TCGTCA	ATC
TTCTCGA	GGAC	17 TGGGGACC	። ርጥሮር ል	יכיבט ד	יסט מידית		190		200
									AGG
	210	220	0	2	30	- :	240		250
ATTCCTA	GGAC	CCCTGCTC	STGTT	ACAG	GCGG	GGTTT	PTCT!	IGTTGA	CAA
CAATCCTC	טטי רארא:	270	) 33.680	2	80		290		300
0.2001	-non	ATACCACAC	SAGTC	TAGA	CTÇG	TGGTG	SACT	CTCTC	AAT
3	310	320	)	3	30	4	340		350
TTTCTAGO	GGG	AGCACCCG	GTGT	CCTG	GCCA	AAATTI	GCAG	TCCCC	720
ב משת מממממ	160	370	)	3	80	3	90		400
CICCAATC	ACTO	CACTAACCI	'CTTG'	rccr	CCAA	TTTGTC	CTGG	TTATC	CT
4	10	420	١.	4	30		40		
GGATGTGT	CTGC	GGCGTTTT	'ATCA	rctt(	CTC	₽ ∩ጥልግጥጥ	ነቸህ የርሞራር	بر سرت میں۔ مرسم میں میں ا	150
									. GC
4	60	470		48	30	4	90	5	00
CTCATCTT	CTTG	TTGGTTCT	TCTG	ACT)	CCAJ	AGGTAT	GTTG	CCCGTI	TG
CCTCTAC	TTCC	520 AGGAACAT	ר א א ריז	ים מים מי	OCONO	5. 20057.0	40	5	50
									CT
5	60	570		. 58	0	5	90	6	00
SCACGACT	CCTG	CTCAAGGA	ACCTO	TATG	TTTC	CCTCT	TGTT	GTTGTA	CA
									•••
ዕ.ልስርርጥጥር (	CONC	620		63	0	6	40	6	50
-4306116	JOHC	GGAAATTG	JACTT	GTAT	TCCC	ATCCC	ATCA	CTTGG	GC
	60	670		68	a	5	۵0	-	^^
TTCGCAA	SATT	CCTATGGG	AGTGG	GCCI	CAGI	CCGTT	PCTC2	/ አጥር:ሮርጥ/	00 Ca
									O.A.

Figure 16

## Angeline Ingrid Bartholomeusz et al. HBV VARIANTS DETECTION AND APPLICATION Docket: 19781 Sheet 22 of 55

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710	720	730	740	750
GTTTACTAGT	GCCATTTGTTCAGT	GGTTCGTAG	GGCTTTCCCC	ACTGTT
760	770	780	790	800
TGGTTTTCAGT	PTATGTGGATGATG	TGGTATTGG	GGGCCAAGTCT	GCACAA
810	820	830	840	850
CATCTTGAATO	CCCTTTTTACCGCT	ATTACCAATT	FTTCTTTTGTC	TTTGGG
860	870	880	890	900
TATACATTTA	ACCMTAATAAAAC	CAAACGTTGC	GGGCTATTCCC	TTAACT
910	920	930	940	950
TTATGGGATAT	GGAATTGGAAGTT	GGGTCCTG(	CECAGGGAAGA	TGGCAG
GGG				

Figure 16 continued

# Angeline Ingrid Bartholomeusz et al. HBV VARIANTS DETECTION AND APPLICATION Docket: 19781 Sheet 23 of 55

Figure 17 Patie	nt E: HBV	polymeras	2	• •
10	20	30	40	50
SSSGHAVELQHIPP	SSARSQSEGE	PILSCWWLQF	RNSKPCSDYC	LSHIVNI
60	70	80	90	100
LEDWGPCTEYGEHH	IRIPRTPARV	TGGVFLVDK	iphnttesrl	VVDFSQE
110	120	130	140	150
SRGSTRVSWPKFAV	PNLQSLTNLI	SSNLSWLSL	VSAAFYHLPI	LHPAAMP
160	. 170	180	190	200
HLLVGSSGLPRYVA	RLSSTSRNIN	YQHGTMQDLH	DSCSRNLYVS	PLTTTAK
210	220	230	240	250
TFGRKLHLYSHPIII	LGFRKI PMGV	GLSPFLMäqf	TSAICSVVRF	AFPHCL
260	270	280	290	300
VFSYVDDVVLGAKSA	<i>Q</i> HLESLFTA	ITNFLLSLGI	HLNXNKTKRW	GYSLNE
MGYGIGSWG				

Figure 17

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Figure 18: Patient E HBsAg 20 30 40 . QPTP1SPPLRDSHPQAMQWNSSTFHQALLDPRVRGLYFPAGGSSSGTVNP 70 80 **VPTTASPISSIFSRTGDPAPNMESTTSGFLGPLLVLQAGFFLLTRILTIP** 130 140 150 QSLDSWWTSLNFLGGAPACPGQNLQSPTSNHSLTSCPPICPGYRWMCLRR 170 180 190 FIIFLFILLCLIFLLVLLDYQGMLPVCPLLPGTSTTSTGPCKTCTTPAQ 220 230 GTSMFPSCCCTKPSDGNCTCIPIPSSWAFARFLWEWASVRFSWLSLLVPF 270 280 VQWFVGLSPTVWFSVMWMMWYWGPSLHNILNPFLPLLPIFFCLWVYI\*TX IKPNVGA

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Figure 19

# Angeline Ingrid Bartholomeusz et al. HBV VARIANTS DETECTION AND APPLICATION Docket: 19781 Sheet 26 of 55

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660	670	680	690 .	700
ACAAAACCTTCGGACG				, ron
		A TOTALICUE	AICCCAICAT	CTTG
710	720	730	740	750
GGCTTTCGCAAGATTC			CC:CHAMCACC	730
	CINIOGGAGI	3GGCC I CAG I	ccentificiti	TGGÇ
760	770	300	300	
			790	900
TCAGTTTACTAGTGCC	ATTTGTTCAG:	rggttcgtag	GGCTTTCCCC	CACT
810	820	830	840	850
GTTTGGCTTTCAGTTA	PATGGATGAT	STEGTATTEG	GGGCCAAGTC	יים ביים מיים ש
•			occount of the	IGIA
. 860	870	880	890	.000
				900
CAACATCTTGAATCCCT	(TTTTACCGC)	GTTACCAAT	lttcttttgt(	CTTT
01.0				
910		930		950
GGGTATACATTTAAACC	CTACTAAAA	TAAACGTTG	GGCTACTCC	CTTA
960	970	980		
ACTTCATGGGATATGTA	ATTGGAAGTT	GGGGTACCT	rg	

Figure 19 continued

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### Figure 20 Patient F Pol Amino acid sequence

10 EDWGPCTEYGEH	20 TRIPRTPARUT	30	40	50
*	THERITANAT	MAGAT TAPP	BUNTLE SEPA/	DESQES
60	70	80	90	100
RGSTHVSWPKFAV	PNLQSLTNLLS	SNLSWLSLD	VSAAFYHLPLH	IPAAMPH
110	120	130	140	150
LLVGSSGLPRYVA	RLSSTSRNINY	QHGTMQDLHI	DSCSRNLYVSI	LLLYKT
160	170	180	190	200
FGRKLHLYSHPII	LGFRKIPMGVG:	LSPFLLAQF	rsaicsvvrra	FPHCLA
210	220	230	240	250
FSYMDDVVLGAKS	VQHLESLFTAV	rnfllslgih	LNPTKTKRWG	YSLNFM
GYVIGSWG				

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#### Figure 21 Patient F HBsAg seq

10	20	30	40	50
MESTTSGFLGPLLV	LQAGFFLLTI	RILTIPQSLDS	SWWTSLNFLGO	SAPTCPG
60	70	80	90	TATTDA
QNLQSPTSNHSPTS	CPPICPGYRW	MCLRRFIIFI	FILLLCLIFI	100
110	120	130	140	150
QGMLPVCPLLPGTS	TTSTGPCKTO	TTPAQGTSME	PSCCCTKPSD	GNCTCI
160 PIPSSWAFARFLWE	170 WASVRFSWLS	180 LLVPFVQWFV	190 . GLSPTVWLSV	200 IWMMWY
210 WGPSLYNILNPFLP	220 LLPIFFCLWV	YI		

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				· ·	
Figure :	22: Patier	nt G ;HBV	nt		
	10	20	30	40	50
TCCGCC	rcctgcctcc	ACCAATCGC	CAGTCAGGAA	GGCAACCTAC	CCGC
	60	70	80	90	100
TCTCTC	CACCTTTGAG	AGACACTCA	TCCTCAGGCC	gtgcagtgga)	CTCC
	110	120	130	140	150
ACAACCI	TTCCACCAAA	CTCTGCAAG	ATCCCAGAGT	GAGGGGCCTG1	ATCT
	160	170	180	190	200
CCCTGCT	GGTGGCTCC	agttcaggaj	ACAGCAAACC	CTGTTCCGACT	'ACTG
	210	220	230 -	240	250
CCTCTCG	CTTATCGTC.	AATCTTCTCC	AGGATTGGGG	SACCCTGCGCT	GAAC
	260	270	280	290	300
ATGGAGA	ACATCACAT	Caggactcci	AGGACCCCTT	CTCGTGTTAC	AGGC
<i>-</i>	310	320	330	340	350
				GCAGAGTCTA	GACT
CGTGGTG	360 Cacaacacacac	370	380	390	400
				CCGTGTGTCT	TGGC
СААААТТ	410 CGCGGTCCC	420	430	440	450
				ACCICCIGIC	
	460 CCTGGTTATO	470 IGCTGGATGT	480	490 TTTTATCATA	500
		•			
TCTTCAT	510 CCTGCTGCTA	520 ATGCCTCATC	- 530 TTCTTCTTGG	540 TTCTTCTGGA	550
					CIMI
	560 IGTTGCCCGT	TTGTCCTCT.	580 AATTCCAGGA	590 TCCTCAACCA	600
				640	
CACGGGA	ACATGCCGAA	CCTGCACGA	630 CTCCTGCTCA	640 Aggaacctct!	650 TGT
		670			
	CTGTTGCTGT	'ACCAAACCT'	TCGGACGGAA	690 ATTGCACCTG1	700 ATT

Figure 22

# Angeline Ingrid Bartholomeusz et al. HBV VARIANTS DETECTION AND APPLICATION Docket: 19781 Sheet 30 of 55

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710	720	730	740	750
CCCATCCCATC	CATCTTGGGCTTTC	GGAAAATTC	CTATGGGAGTG	GGCCTC
760	770	780	790	800
AGCCCGTTTCT	CCTGGCTCAGTTT	ACTAGTGCC	ATTTGTTCAGT	GGTTCG
810	820	830	840	850
TAGGGCTTTCC	CCCACTGTTTGGC	TTTCAGTTA	Patggatgatg	TGGTAT
· 860	870	880	890	900
TGGGGGCCAAG	TCTGTACAGCATC	TTGAGTCCC	FTTTTACCGCT	GTTACC
910	920	930	940	950
AATTTTCTTTT	GTCTTTGGGTATA	CATTTAACC	CTAACAAAAC	Aaagag
960	970 CTCTAAATTTTAT	980	990	1000
1010	1020 GAACACATTATAC	1030	1040	

Figure 22 continued

# Angeline Ingrid Bartholomeusz et al. HBV VARIANTS DETECTION AND APPLICATION Docket: 19781 Sheet 31 of 55

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Figure	23	Patient	G	HBV	POT.
94	~ ~	T T - 11 -	J	nav	FUL

10	20	30	40	50
EDWGPCAEHGEHHI	RTPRTPSRV	TGGVFLVDKNE	HNTAESELV	UDESOES
				. 515013
60	70	80	00	100
BCNYRVSWDKEAUD	NT OFT MALE	CCD1 CD2 c2 c4	90	100
RGNYRVSWPKFAVP	итбартитг	SSOFSMTRTDA	Saafyhipli	HAMMAH
_ 1.1				
ļ10	120	130	140	150
LLVGSSGLSRYVAR	LSSNSRILN	HOHGNMPNTAD	SCEDNI VIZE	77770
			OCOMME! A 21	rrrt I G.I.
160	170	100		
		180	190	200
FGRKLHLYSHPIIL	GERKIPMGV(	GLSPFLLAQFT	SAICSVVRRA	FPHCLA
• •				
210	220	230 -	240	250
FSYMODVVLGAKSV	OHLESTETAL	TONETT OF CTU	7 MD11/M717-7-4	230
	ZDOODL IN	THEBPSTOTH	PILBUKIKKMG	YSLNFM
CVIIICEVA				
GYVIGSYG				

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Figure 24: Patient G AbsAg

10 20 30 40 50

MENITSGLIGPLLVLQAGFFLLTRILTIPQSLDSWWTSLSFLGGTTVCLG

60 70 80 90 100

QNSRSPTSNHSPTSCPPTCPGYRWMYLRRFIIFLFILLLCLIFLLVLLDY

110 120 130 140 150

QGMLPVCPLIPGSSTTSTGTCRTCTTPAQGTSMYPSCCCTKPSDGNCTCI

160 170 180 190 200

PIPSSWAFGKFLWEWASARFSWLSLLVPFVQWFVGLSPTVWLSVIWMMWY

210 220 WGPSLYSILSPFLPLLPIFFCLWVYI

## Angeline Ingrid Bartholomeusz et al. HBV VARIANTS DETECTION AND APPLICATION Docket: 19781 Sheet 33 of 55

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#### Figure 25 Patient H nt seq

			•		
	10	20 .	30	40	50
CGCCTCCI	GCCTCCAC	CAATCGCCAG	TCAGGAAGG	CAGCCGACCC	ACTG
	0.00				
O'CTCC N CC	60	70	80	90	100
ICICCACC	TTTGAGAG	ACACTCATCC	TCAGGCCGT	CAGTGGAACT	CCAC
. 1	.10	120	130	1.40	
		TZU CTGCAAGATC	130 COCOCOCO	140 SAGGCCTGTAT	150
		OIGCAMOAIC	CCAGAGIGAG	AGGCCTGTAT	TTCC
1	. 60.	170	180	190	200
CTGCTGGT	GGCTCCAG	TTCAGGAACA	GTAAACCCTG	TTCCGACCAC	TGCC
					- 000
_	10	220-	230	240 .	250
TCTCCCTT	'ATCGTCAA'	PCTTCTCGAG	GATTGGGGAC	CCTGCGCTGA	ACAT
•	60	270			
		_4/U ~CDBBCCBBC	280	290	300
OGNORACA	TORCAL CA	3GATTCCTAG	GACCCCTTCT	CGTGTTACAG	GCGG
3	10	320	330	340	350
GGTTTTTC	TTGTTGAC		ACAATACCGC	AGAGTCTAGA:	ריירכ
		•			0100
-	60		380	390	400
TGGTGGAC	TTCTCTCAC	STTTTCTAGG	GGAAACCACC	GTGTGTCTTG	GCCA
					,
	10	420	430	440	450
MATICOC.	AGI CCCCA	CCICCAATC	ACTCACCAAC	CTCCTGTCCT	CCAA
4	60	470	480	490	۲۸۵
CTTGTCCT	GGTTATCGC	TGGATGTGT	TGCGGCGTT'	TTATCATATT	500
					2010
	10	520	530	540	550
TTCATCCT	GCTGCTATG	CCTCATCTT	CTTGTTGGTT	CTTCTGGACT!	ATCA
	60 BCCCCC	570	580	590	600
AGGIAIGI	rececern	GTCCTCTAAT	TCCAGGATC	CTCAACCACCA	<b>AGCA</b>
6.	10	620	630		
		*************************************	COU COUCCUCANCO	640 Saacctctato	650
		- somounci(	CIGCICAMGC	SARCCICTATE	TAT
6	60	670	680	690	700
CCCTCCTG	ITGCTGTAC	CAAACCTTC	GACGGAAAT1	GCACCTGTAT	TCC

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716 CATCCCATCATC	720 PTGGGCTTTCGC			750 GCTCAG
760 CCCGTTTCTCATO		780 TAGTGCCAT	790 TTGTTCAGTGG	800 STTCGTA
810 GGGCTTTCCCCC	820 - ACTGTTTGGCTT	830 TCAGTTATG	840 TGGATGATGTG	850 GTAȚTG
8 60 GGGGCCAAGTCT		880 GAGTCCCTT	890 ITTACCGCTGT	900 TACCAA
910 TTTTCTTTTGTCT		930 TTTAAACCC		950 AAAGAT
960 GGGGTTACTCTT1		980 GGTATGTTA		1000 GGGTCC
1010 TTGCCACAAGAAC	1020 CACATCGTACAA	AAA		

Figure 25 continued

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Figure 26: Fatient H HBV pol

260 GYVIGCYGSLPQEH

20 30 40 EDWGPCAEHGEHHIRIPRTPSRVTGGVFLVDKNPHNTAESRLVVDFSQFS 70 80 90 RGNHRVSWPKFAVPNLQSLTNLLSSNLSWLSLDVSAAFYHIPLHPAAMPH 130 140 LLVGSSGLSRYVARLSSNSRILNHQHGTMPNLHDSCSRNLYVSLLLLYQT 170 180 190 FGRKLHLYSHPIILGFRKIPMGVGLSPFLMAQFTSAICSVVRRAFPHCLA 220 230 240 FSYVDDVVLGAKSVSHLESLFTAVTNFLLSLGIHLNPNKTKRWGYSLNFM

Figure 26

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### Angeline Ingrid Bartholomeusz et al. HBV VARIANTS DETECTION AND APPLICATION Docket: 19781 Sheet 36 of 55

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Figure 27: Patient H HBsAg

10 20 30 40 50 MENITSGFLGPLLVLQAGFFLLTRILTIPQSLDSWWTSLSFLGETTVCLG

60 70 80 90 100 QNSQSPTSNHSPTSCPPTCPGYRWMCLRRFIIFLFILLLCLIFLLVLLDY

110 120 130 140 150 QGMLPVCPLIPGSSTTSTGPCRTCTTPAQGTSMYPSCCCTKPSDGNCTCI

160 170 180 190 200 PIPSSWAFAKFLWEWGSARFSWLSLLVPFVQWFVGLSPTVWLSVMWMMWY

210 220 WGPSLYRILSPFLPLLPIFFCLWVYI

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Figure 28 Patient I HBV nt seq

			•		
C) ) CT	10	20	30	40	50
CAACI	rerecte	GTTATCGCTGG	ATGTGTCTGC	GGCGTTTTAT	CATATTO
	60	70	09	90	100
CTCTT	CATCCTG	CTGCTATGCCTC	ATCTTCTTG	TTGGTTCTTC	TGGACTA
	110	120	130	140	150
TCGAG	GTATGTT	SCCCGTTTGTCC	TCTACTTCC	AGGATCTTCA	ACCACCA
	160	170	180	190	200
GCACG	GGTCCAT	GCAGAACCTGCA	CGACTCCTG	CTCAAGGAAC	CTCTATG
	210	220	230	240	250
TATCC	CTCATGTT	GCTGTACCAAA	CCTTCGGAC	GGAAATTGCAG	CTGTAT
	260	270	280	290	300
TCCCA	CCCATCA	TCCTGGGCTTT	CGGAAAATT	CCTATGGGAG1	rogecct Todogo:
		320			
CAGCC	CGTTTCTC	ATGGCTCAGTT	TACTAGTGC	CATTTGTTCAG	330 TGGTTC
	360 ·	. 370 ·	380	200	400
GTAGGG	CTTTCCC	CCATTGTTTGG	CTTTCAGTT/	390 ATGTGGATGAT	GTGGTA
		420			
TTGGGG	GCCAAGT	CTGTATCGCAT	430 CTTGAGTCC	440 CTTTTTACCGC	450 TGTTAC
САЛТТ	TCTTTTG	470 TCTCTGGGTAT	480 Acatttaaa	490 CCTCACAAAA	500 AAAAA
GATGGG	GTTACTC	520 TTTACATTTCA	530 Igggctatgt	540 Categatet	550 TATECC
					111000
TCTTTG	560 CCAC				

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Figure 29 Patient I HBV pol

10 20 30 40 50

NLSWLSLDVSAAFYHIPLHPAAMPHLLVGSSGLSRYVARLSSTSRIFNHQ

60 70 80 90 100

HGSMQNLHDSCSRNLYVSLMLLYQTFGRKLHLYSHPIILGFRKIPMGVGL

110 120 130 140 150

SPFLMAQFTSAICSVVRRAFPHCLAFSYVDDVVLGAKSVSHLESLFTAVT

160 170 180
NFLLSLGIHLNPHKTKRWGYSLHFMGYVIGCYGSLP

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39 of 55 30 TCPGYRWMCLRRFIIFLFILLLCLIFLLVLLDYRGMLPVCPLLPGSSTTS

TGPCRTCTTPAQGTSMYPSCCCTKPSDGNCTCIPIPSSWAFGKFLWEWAS

120 ARFSWLSLLVPFVQWFVGLSPIVWLSVMWMMWYWGPSLYRILSPFLPLLP

160 170 180 IFFCLWVYI\*

Figure 30 Patient I: HBsAg

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Figure 31

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-710 720 740 CCCATCCCATCATCTTGGGCTTTCGCAAGATTCCTATGGGAGTGGGCCTC 770 780 790 · AGTCCGTTTCTCCTGGCTCAGTTTACTAGTGCCATTTGTTCAGTGGTTCG 830 840 850 TAGGGCTTTCCCCCACTGTTTGGCTTTCAGTTATATGGATGATGTGGTAT 870 880 890 TGGGGGCCAAGTCTGTACAACATCTTGAATCCCTTTTTACCGCTGTTACC 920 930 940 AATTTTCTTTTGTCTTTGGGTATACATTTAAACCCTACTAAAACTAAACG 980 990 1000 TTGGGGCTACTCCCTTAACTTCATGGGATATGTAATTGGAAGTTGGGGTA 1020 CCTTACCACAGGAACATATTGTACACAAA

Figure 31 continued

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Figure 32 Patient J HBV pol

10 20 30 40 50 EDWGPCTEYGEHNIRIPRTPARVTGGVFLVDKNPHNTTESRLVVDFSQFS

60 70 80 90 100 RGSTHVSWPKFAVPNLQSLTNLLSSNLSWLSLDVSAAFYHLPLHPAAMPH

110 120 130 140 150 LLVGSSGLPRYVARLSSTSRNINYQHGTMQDLHDSCSRNLYVSLLLLYKT

160 170 180 190 200 FGRKLHLYSHPIILGFRKIPMGVGLSPFLLAQFTSAICSVVRRAFPHCLA

210 220 230 240 250 FSYMDDVVLGAKSVQHLESLFTAVTNFLLSLGIHLNPTKTKRWGYSLNFM

260 GYVIGSWGTLPQEHIVHK

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Figure 33. Patient J HBsAg

10 20 30 40 50 MESTTSGFLGPLLVLQAGFFLLTRILTIPQSLDSWWTSLNFLGGAPTCPG

60 70 80 90 100 QNLQSPTSNHSPTSCPPICPGYRWMCLRRFIIFLFILLLCLIFLXVLLDY

110 120 130 140 150 QGMLPVCPLLPGTSTTSTGPCKTCT1PAQGTSMFPSCCCTKPSDGNCTCI

160 170 180 190 200 PIPSSWAFARFLWEWASVRFSWLSLLVPFVQWFVGLSPTVWLSVIWMMWY

210 220 WGPSLYNILNPFLPLLPIFFCLWVYI

Figure 33

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Figure 34 Patient K HBV nt

10	20	30	40	50
CTCCTCCTGC	CTCCACCAATC	GGCAGTCAG	GAAGACAGCC!	TACACCCATC
60	. 70	90	0.0	100
TCTCCACCTCT				100 CANCTCCAG
			occarocao.	Judici CCAG
110	120	130	140	150
CACATTCCAC	Caagetetget	'AGATCCCAG	AGTGAGGGGC	CTATACTTTC
160	170	190	190	200
CTGCTGGTGG	CTCCAGTTCAG	GAACAGTAA	T PU ACCCTGTTCC	002 CORPORTORS
			•	
	220			
TCTCCCATATO	CGTCAATCTTC	TCGAGGACT	GGGGACCCTG	CACCGAATAT
260	270	290	200	300
GGAGAGCACC	CATCAGGATT	CCTAGGACC	Z 50 CCTGCTCGTGT	UUC TRACAGETT
			340	
GGTTTTTCTTG	sttgacaagaa	TCCTCACAA	TACCACAGAG	CTAGACTCG
360	370	380	ne e	400
TGGTGGACTT	TCTCAATTTT	CTAGGGGGA	GCACCCACGT	STCCTGGCCA
410	420	430	440	450
AAATTTGCAGT	CCCCAACCTC	CAATCACTC	ACCAACCTCTT	GTCCTCCAA
460	470	480	490	500
TTTGTCCTGGT	TATCGCTGGA	TGTGTCTGC	GGCGTTTTAT	CATCTTCCTC
510	520	530	540	550
TTCATCCTGCT	GCTATGCCTC	ATCTTCTTG	TTGGTTCTTCT	GGACTACCA
560	570	· 580·	590	600
AGGTATGTTG				
	620	630	640	650
CGGGACCATGO	AAGACUTGCA	CGATTCCTG	CTCAAGGAACC	TCTATGTTT
660	670	680	690	700
CCCTCTTGTTG				

Figure 34

## Angeline Ingrid Bartholomeusz et al. HBV VARIANTS DETECTION AND APPLICATION Docket: 19781 Sheet 45 of 55

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710 720 730 750 740 CATCCCATCATCTTGGGCTTTCGCAAGATTCCTATGGGAGTGGGCCTCAG 780 790 TCCGTTTCTCCTGGCTCAGTTTACTAGTGCCATTTGTTCAGTGGTTCGTA 820 830 GGGCTTTCCCCCACTGTTTGGCTTTCAGTTATATGGATGATGTGGTATTG 870 880 890 GGGGCCAAGTCTGTACAACATCTTGAATCCCTTTTTACCGCTGTTACCAA 930 TTTTCTTTTGTCTTTGGGTATACATTTAAACCCTRCTAAAACCAAACGTT 960 990 1000 GGGGTTACTCCCTTAACTTCATGGGATATGTAATTGGAAGTTGGGGTACC .1010 1020 1030 TTACCACAGGAACATATTGTACACAAAATCAAACA

Figure 34 continued

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. Figure 35 Patient K HBV pol

20 30 40  ${\tt SSCLHQSAVRKTAYTHLSTSKRQSSSGHAVELQHIPPSSARSQSEGPILS}$ 70 80 90 CWWLQFRNSKPCSDYCLSHIVNLLEDWGPCTEYGEHHIRIPRTPARVTGG 140 VFLVDKNPHNTTESRLVVDFSQFSRGSTHVSWPKFAVPNLQSLTNLLSSN 170 180 190 LSWLSLDVSAAFYHLPLHPAAMPHLLVGSSGLPRYVARLSSTSRNINYQH 220 230 240 GTMQDLHDSCSRNLYVSLLLLYKTFGRKLHLYSHPIILGFRKIPMGVGLS 270 280 PFLLAQFTSAICSVVRRAFPHCLAFSYMDDVVLGAKSVQHLESLFTAVTN 310 320 330 FLLSLGIHLNPXKTKRWGYSLNFMGYVIGSWGTLPQEHIVHKIK

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Figure 36 Patient K HbsAg 10 20 30 40 PPASTNRQSGRQPTPISPPLRDSHPQAMQWNSSTFHQALLDPRVRGLYFP 80 AGGSSSGTVNPVPTTASPISSIFSRTGDPAPNMESTTSGFLGPLLVLQAG 130 FFLLTRILTIPQSLDSWWTSLNFLGGAPTCPGQNLQSPTSNHSPTSCPPI 180 190 · 170 CPGYRWMCLRRFIIFLFILLLCLIFLLVLLDYQGMLPVCPLLPGTSTTST 230 240 GPCKTCT1PAQGTSMFPSCCCTKPSDGNCTC1P1PSSWAFARFLWEWASV 270 280 290 RESWLSLLVPEVQWEVGLSPTVWLSVIWMMWYWGPSLYNILNPELPLLPI

330

320

FFCLWVYI\*TLLKPNVGVTPLTSWDM\*LEVGVPYHRNILYTKSN

Figure 36

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# Angeline Ingrid Bartholomeusz et al. HBV VARIANTS DETECTION AND APPLICATION Docket: 19781 Sheet 48 of 55

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Figure 37 Patient L HBV nt

	20	30	40	50
CAGTCCGGAAGGC	AGCCTACTCC	TTATCTCCA	CCTCTAAGGG	טט מרארידר א
				.01.01.01
60	70	80	90	100
TCCTCAGGCCATG	:AGTGGAACT(	CACCACTTT	CCATCAAACT	TTCAAG
110		130	140	150
ATCCCAGAGTCAGG	GCTCTGTACT	TTCCTGCTG	GTGGCTCCAG1	TCAGGA
160	170	180	100	
ACAGTGAGCCCTGC		CCCMCMCCC TOU	190	200
	A CHOPPHINCI	GCCTCTGCC	ATATOGTOAA(	CTTCTC
210	220	230	240	250
GAAGACTGGGGACC	CTGTACCGAA	CATGGAGAA	CATCGCATCAG	ひとろ
				,0,10100
260	270		290	300
TAGGACCCCTGCTC	GCGTTACAGG	CGGGGTTTT	TCTCGTTGACA	AAAATC
310	320	330	340	350
CTCACAATACCACA	GAGTCTAGAC	TCGTGGTGG	acttctctcaa	TTTTCT
360	370	380	300	
AGGGGGAACACCCG		200 ንግሞሞፈፈፈግግ	390 300 - 300 - 300 - 300 - 300 - 300 - 300 - 300 - 300 - 300 - 300 - 300 - 300 - 300 - 300 - 300 - 300 - 300 - 300	400
		CCISTAGLIC	3CAGICCCAAA	ICTCCA
410	420	430	440	450
GTCACTCACCAACT	TGTTGTCCTC	CAATTTGTC		TGGATG
460	470		490	500
TGTCTGCGGCGTTT	TATCATCTTC	CTCTGCATC	CTGCTGCTATG	CCTCAT
510 CTMCTTCTTCCTTC	520	530	540	550
CTTCTTGTTGGTTC	TTCTGGACTA	TCAAGGTATO	STIGCCCGTIT	GTCCTC
560	570	580	590	600
TAATTCCAGGATCA		GCACCGGACC	ひとて ころかのことであること	600
		CGGACC	m. GCMGMMCC.	LGCHCG
610	620	630	640	650
ACTCCTGCTCAAGG	AACCTCTATG	TTTCCCTCAT	GTTGCTGTAC	AAAACC

Figure 37

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	670		690	700
TACGGACGGAA	ACTGCACCTG1	PATTCCCATC	CCATCATCTT	GGGCTTTCG
710		730		750
CAAAATACCTA	TGGGAGTGGG	CTCAGTCC	STTTCTCTTGG	CTCAGTTTA
760	770		790	800
CTAGTGCCGTT	TGTTCAGTGG1	TCGTAGGGC	TTTCCCCCAC	TGTCTGGCT
- 810	820	830	840	850
TTCAGTTATAT	ggatgatgtg0	STATTGGGGG	CCAAGTCTGT	ACAACATCT
860	870	880	. 890	900
TGAGTCCCTTT				
910	920	930	940	950
ATTTAAACCCT		-		- • •
960	970	980		
GGATATGTAAT				

Figure 37 continued

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Figure 38. Patient L Pol

20 10 30 40 EDWGPCTEHGEHRIRTPRTPARVTGGVFLVDKNPHNTTESRLVVDFSQFS 70 90 100 RGNTRVSWPKFAVPNLQSLTNLLSSNLSWLSLDVSAAFYHLPLHPAAMPH 120 130 140 LLVGSSGLSRYVARLSSNSRIINHQHRTMQNLHDSCSRNLYVSLMLLYKT 160 170 180 190 YGRKLHLYSHPIILGFRKIPMGVGLSPFLLAQFTSAVCSVVRRAFPHCLA 220 230 FSYMDDVVLGAKSVQHLESLYAAVTNFLLSLGIHLNPHKTKRWGYSLQFM GYVIGGWG

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Figure 39 Patient L HBsAg

10 20 30 40 50
MENIASGLLGPLLALQAGFFSLTKILTIPQSLDSWWTSLNFLGGTPVCLG

60 70 80 90 100
QNSQSQISSHSPTCCPPICPGYRWMCLRRFIIFLCILLLCLIFLLVLLDY

110 120 130 140 150 QGMLPVCPLIPGSSTTSTGPCRTCTTPAQGTSMFPSCCCTKPTDGNCTCI

160 170 180 190 200 PIPSSWAFAKYLWEWASVRFSWLSLLVPFVQWFVGLSPTVWLSVIWMMWY

210 220 WGPSLYNILSPFMPLLPIFFCLWVYI

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CCTG	10 CTGGTGGC	20 TCCAGTTCAGGA	30 ACAGTAAAC	40 CCTGTTCCGA	50 CTACTGC
	60	70	80	90	100
CICI	CCCTTATC	GTCAATCTTCTC	GAGGATTGG	GGACCCTGCG	CTGAACA
TGGA	110 GAACATCA	120 CATCAGGATTCC	130 TAGGACCC	140 TTCTCGTGTT	150 ACAGGCG
	160	170	180	190	200
GGGTT	TTTCTTG	TTGACAAGAATC	CTCACAATA	CCGCAGAGTC	TAGACTC
CTCC1	210	220	230	240	250
61001		TCTCAATTTTCG			
AAAA1	260 TCGCAGT	270 CCCCAACCTCCA	280 ATCACTCAC	290 CAACCTCCTG	00E
ACTT	310 TCCTGGT	320 TATCGCTGGATG	330 TGTCTGCGG	340 CGTTTTATCA	350 האדדרכים
		•			
CTTCA	JOU LTCCTGCT	370 GCTATGCCTCAT	380 CTTCTTGTT	390 GGTTCTTCTG	400 SACTATC
RAGGT	410 ATGTTGC	420 CCGTTTGTCCTC	430 TAATTCCAG	440 GATCCTCAWC	450 CACCAGC
	460	470	480	490	500
ACGGG	ACCATGC	CGAACCTGCATG.	actactgct	CAAGGAACCT	CTATGTA
	510	520	530	540	550
TCCCT	CCTGTTG	CTGTACCAAACC	TACGGACGG	<b>AAATTGCACC</b> 1	CGTATTC
	560	570	580	590	600
CCATC	CCATCAT	CCTGGGCTTTCG	Gaaaattcc	Tatgggagtg	SGCCTCA
	610	620	630	640	650
GCCCG	TTTCTCC	<b>I</b> GGCTCAGTTTA	CTAGTGCCA	TTTGTTCAGT	GTTCGT
	660	670	680	690	700
AGGGC	TTTCCCC	CACTGTTTGGCT:	ITCAGTTAT.	atggatgatgt	GGTATT
		720	730	740	750
GGGGG	CCAAGTC'	PGTAYMGCATCT!	PGAGTCCCT	ITTTACCGCTC	TTACCA
	760	770	780	790	800
ATTTT	CTTTTGT	CTTTGGGTATAC	ATTTAAACC	CTAACAAAACA	LAAGAGA
	810	820	830	840	850
TGGGG	TTACTCT	CTGAATTTTATG	GGTTATGTC	attggaagtta	TGGGTC
	860	870	880	890	900
CTTGC	CACAAGAI	ACACATCATACA	AAAAATCAA	agaatgttt <i>a</i>	GAAAAC

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30 20 CWWLQFRNSKPCSDYCL5LIVNLLEDWGPCAEHGEHHIRIPRTPSRVTGG 70 80 90 VFLVDKNPHNTAESRLVVDFSQFSRGNYRVSWPKFAVPNLQSLTNLLSSN 120 140 LSWLSLDVSAAFYHXPLHPAAMPHLLVGSSGLSRYVARLSSNSRYLXHQH 170 180 190 GTMPNLHDYCSRNLYVSLLLLYQTYGRKLHLYSHPIILGFRKIPMGVGLS 220 230 240 PFLLAQFTSAICSVVRRAFPHCLAFSYMDDVVLGAKSVXHLESLFTAVTN 270 280 FLLSLGIHLNPNKTKRWGYSLNFMGYVIGSYGSLPQEHIIQKIKECFRK

### Figure 41

10 20 PAGGSSSGTVNPVPTTASPLSSIFSRIGDPALNMENITSGFLGPLLVLQA .70 90 **GFFLLTRILTIPQSLDSWWTSLNFRGGTTVCLGQNSQSPTSNHSPTSCPP** 120 130 140 TCPGYRWMCLRRFIIFLFILLLCLIFLLVLLDYXGMLPVCPLIPGSSXTS 170 180 TGPCRTCMTTAQGTSMYPSCCCTKPTDGNCTCIPIPSSWAFGKFLWEWAS 220 230 ARFSWLSLLVPFVQWFVGLSPTVWLSVIWMMWYWGPSLYXILSPFLPLLP IFFCLWVYI\*

Figure 42

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		- · · · ·			
	.0	20	30 .	40	50
CTTTCACCA	AACTCTG	CAAGATCCCC	CTGCTGGTGG	CTCCAGTTCA	LGGAA
	0 "CTGTTCC	70 32000000000		90	100
CAGIAMACC	C1G110C	MCIACIGCC	TCTCCCTTAT	CGTCAATCTT	CTCG
11		120	130	140	150
AGGATTGGG	GACCCTG	CGCGGAACAT	GGAGAACATC	ACATCAGGAT	TCCT
16		170 "Tacaccocc	180	190	200
ROGRECEEL	1010010	TYCHGGCGG	GGTTTTTCTT	GTTGACAAGA	ATCC
21		220	230	240	250
TCACAATAC	CGCAGAG1	CTAGACTCG	<b>TGGTGGACTT</b>	CTCTCAATTT	TCTA
26	0	27.0		_0.	
26 GGGGGAACT		270 TCTTGGCCN:		290 TCCCCAACCT	300
0000011.01		TOTTOGCCA	HAAT TOGCAG	ICCCCAACCT	CCAA
31		320	330	340	350
TCACTCACC	AACCTCCI	GTCCTCCAA	CTTGTCCTGG	TTATCGCTGG	ATGT
ಅಲ ವಿವಾದವರ್ಗವಿಗಾ	U ርጥየጥጥ ልጥር	370 `ATCTTCCTC	380 PTCD/PCCTCC	390 TGCTATGCCT	400
01010000	0111111		ITCAICCIGC	IGCTATGCCT	CATC
41	0	420	430	440	450
TTCTTGTTG	GTTCTTC1	'GGACTATCRI	AGGTATGTTG	CCCGTTTGTC	CTCT
A C	0		400		
• •	o Atcctcae	470 CCACCAGCA(	TGGGACCATG	490° CCGAACCTGC	500
			OCCALC	CCGAACCIGC	A1 GA
510		520	530	540	550
CTACTGCTC	AAGGAACC	TCTATGTATO	CCCCCCTGTT	GCTGTACCAA	ACCT
560	n	570	580	600	400
ACGGACGGA	AATTGCAC	CTGTATTCC	CATCCCATCA'	590 ICCTGGGCTT:	600 TCGG
			•		i CGG
610		620	630	640	650
AAAATTCCT	atgggagt	'GGGCCTCAG(	CCCGTTTCTC	CTGGCTCAGT	rtac
660	n	670	690	590	700
			GGCTTTCCC	690 CCACTGTTTG	700 3000
710	)	720	730	740	750
TCAGTTATAT	IGGATGAT	GTGGTATTGG	GGGCCAAGT	CTGYACAGCA	CTT
760	1	770	780	7.00	
				790 ICTTTGGGTAT	008
				CITIGGGIA	IACA
810		820	830	840	850
TTTAAACCCT	raacaaaa A	CAAAGAGATO	GGGTTACTC?	rctgaatttt <i>i</i>	ATGG
860	,	070	000	222	
		870 Tateceteet	980 ידהרראראאה:	890 \ACACATCAT?	900
				TIMO I MORE	NA
910	)				
AAAATCAAA	AAS				

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20 30 LSPNSARSPCWWLQFRNSKPCSDYCLSLIVNLLEDWGPCAEHGEHHIRIP 80 90 100 RTPSRVTGGVFLVDKNPHNTAESRLVVDFSQFSRGNYRVSWPKFAVPNLQ 130 140 SLTNLLSSNLSWLSLDVSAAFYHLPLHPAAMPHLLVGSSGLSRYVARLSS 170 180 190 NSRILNHQHGTMPNLHDYCSRNLYVSLLLLYQTYGRKLHLYSHPIILGFR 210 220 230 KIPMGVGLSPFLLAQFTSAICSVVRRAFPHCLAFSYMDDVVLGAKSXQHL ` 280 270 290 ESLFTAVTNFLLSLGIHLNPNKTKRWGYSLNFMGYVIGSYGSLPQEHIIQ KIKE

#### Figure 44

30 **FHQTLQDPPAGGSSSGTVNPVPTTASPLSSIFSRIGDPARNMENITSGFL** 80 GPLLVLQAGFFLLTRILTIPQSLDSWWTSLNFLGGTTVCLGQNSQSPTSN 120 130 HSPTSCPPTCPGYRWMCLRRF11FLF1LLLCL1FLLVLLDYXGMLPVCPL 170 180 190 IPGSSTTSTGPCRTCMTTAQGTSMYPSCCCTKPTDGNCTCIPIPSSWAFG 220 230 240 KFLWEWASARF9WLSLLVPFVQWFVGLSPTVWLSVIWMMWYWGPSLXSIL 260 SPFLPR\*PIFFCLWVYI\*

Figure 45

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